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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/599,928

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EXAMINER

HEYER, DENNIS

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/599,928	Applicant(s) ROSER, BRUCE JOSEPH	
	Examiner DENNIS HEYER	Art Unit 1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 03 June 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 and 12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 3, 2010 has been entered.

Acknowledgement is made of Applicant's remarks filed June 3, 2010.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of Claims

Claims 1 – 10 and 12 are currently pending.

Claim rejections – 35 USC § 112 – 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 – 10 and 12 are rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "in which at least one component comprises a liquid hydrofluorinated ether....". There is insufficient antecedent basis for this limitation in these claims. The term "component" has not been defined in the claim. The language "in which at least one component" is confusing because it is unclear whether the language references "components" of the liquid or "components" of the "formulation". For the purpose of examination on the merits with respect to the prior art, the term 'component' will be considered to refer to any one of the ingredients previously recited in the claim, i.e. 'an active ingredient', 'glassy or amorphous particles' and 'a liquid'.

Claim rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 – 10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roser, J.R. in US patent 6,190,701 (published: 02/20/2001; IDS

US Patent Cite No. 1; previously applied in the Office Action mailed 12/3/2009) in view of Johnson, K.A. in US patent 5,376,359 (published: 12/27/1994; previously applied in the Office Action mailed 12/3/2009).

Instant Claim 1 recites a formulation comprising an active ingredient preserved in a glassy or amorphous particle and suspended in a liquid. Instant Claim 1 also requires that at least one of the active ingredient, particles or liquid comprise a liquid hydrofluorinated ether.

Roser teaches a composition comprising a first component comprising a bioactive compound and sugar glass microparticles, and a second component, which comprises a biocompatible liquid perfluorocarbon (Abstract; instant Claim 1).

Roser teaches, in Example 2 (column 9), a suspension of alkaline phosphatase (a bioactive agent) immobilized in mannitol-based (sugar glass; instant Claim 2) microspheres (particles) in the liquid perfluorodecalin (a perfluorocarbon, instant Claim 5). Roser teaches the alkaline phosphatase/mannitol particles retain close to 100% of their activity after 30 days (i.e. the enzyme is stabilized and its activity is preserved; instant Claim 1).

Roser teaches formulations in which additional components are added to the particles to provide a density in which the particles are stably dispersed (column 7, lines 16 – 18; Claim 13; instant Claim 3). Roser teaches the liquid may be blended with different components to achieve the desired density (Column 5, lines 49 – 56; instant Claim 4).

Roser teaches formulations in which the bioactive agent is a vaccine (Column 5, lines 40 – 44; Claim 17; instant Claim 6).

Roser teaches the particles may be made by the conventional techniques of spray-drying, freeze-drying and milling (grinding) (column 5, lines 65 – 67; column 6, lines 6 – 7; Example 5; instant Claims 7 – 9).

Roser teaches the method step recited in instant Claim 10 in which fluorinated solvents are selected in order to provide the required density matching (column 9, lines 20 – 27).

As noted above, Roser teaches compositions comprising a perfluorocarbon liquid. Further, Roser teaches if minor aggregation of the suspended sugar glass particles is a problem, small amounts of a fluorohydrocarbon (FHC) surfactant can be advantageously added to the perfluorohydrocarbons (PFC) liquid (column 6, lines 8 – 16). However, Roser does not teach compositions comprising a liquid hydrofluorinated ether (HFE) (instant Claim 1) or a hydrofluoroether or hydrofluoropolyether (instant Claim 12).

Johnson teaches a stabilized aerosol drug formulation comprising a suspension of a solid particulate drug composition with a fluoropolymer in a liquid fluorocarbon aerosol propellant (column 2, lines 17 – 37). Johnson teaches that drugs formulated as fine suspensions have a tendency to aggregate (“flocculate” or “clump up”) (column 1, lines 42 – 44).

Johnson teaches that the combination of a fluoropolymer in a liquid fluorocarbon aerosol propellant resists flocculation of the suspended drug particles and

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thus, stabilizes the suspension (column 6, Example 1, lines 47 – 53). Johnson teaches the chemical structures of 34 fluorocarbon aerosol propellants including at least eight that are hydrofluoroethers (HFE's, hydrofluoroethers are considered to be indistinct from 'hydrofluorinated ether') (column 2, lines 41 – 64; instant Claims 1 and 12).

Johnson teaches that fluoropolymers include fluoropolyethers in which the term 'perfluorinated' is defined to mean that all, or essentially all, of the hydrogens on the fluoroether polymer are replaced with fluorine. Accordingly, in light of the teaching of 'essentially all of the hydrogens' are replaced by fluorine, one can reasonably construe that hydrofluoro polyethers (HFE's; instant Claim 12), in which at least some of the hydrogens are not replaced by fluorine, are also within the scope of the stabilized suspension compositions of Johnson.

It would have been *prima facie* obvious to one skilled in the art, to modify at least one 'component' (see 112 2nd paragraph rejection above) in the formulation of Roser with a liquid hydrofluorinated ether. One would have been motivated to do so because Johnson teaches that compositions comprising a particulate solid drug (active agent) and a fluoroetherpolymer suspended in a liquid hydrofluorinated ether (HFE) aerosol propellant form stable suspensions by helping to prevent flocculation of the suspended drug particles. Accordingly, there would have been a reasonable and predictable expectation that adding one of the fluoropolyethers or a liquid hydrofluorinated ether propellant would also stabilize the suspended active agent glassy or amorphous particles of Roser.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 – 6, 10 and 12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1 – 4, 13 and 16 – 18 of Roser in U.S. Patent 6,190,701, in view of Johnson in US patent 5,376,359.

Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons below:

The instant Claims and those in the copending Patent each claim a composition (a formulation) comprising a bioactive agent (a vaccine) and sugar glass particles suspended (dispersed) in a liquid. The difference between the instant Claims and those in the copending patent is that the copending Patent Claims require a perfluorocarbon liquid and the instant Claims require a liquid hydrofluorinated ether.

Johnson teaches a composition comprising a solid particulate drug composition and a fluoropolyether that forms a stable suspension in a liquid fluorocarbon aerosol propellant (Abstract). The Johnson reference also teaches that such compositions may comprise hydrofluorinated ethers and hydrofluorinated polyethers. Johnson teaches that compositions comprising hydrofluorinated ethers and hydrofluorinated polyethers stabilize the suspension of drug particles and thus prevent aggregation or flocculation. Thus, it would have been *prima facie* obvious to one skilled in the art, to modify the perfluorohydrocarbons in the claimed suspensions of Roser with the hydrofluorinated polyethers and hydrofluorinated ethers of Johnson with a reasonable and predictable expectation of stabilizing the drug particle suspension.

Response to Arguments

Applicant's arguments filed June 3, 2010 with respect to the rejection under 35 U.S.C 103(a) of Claims 1 – 10 and 12 as being unpatentable over Roser, J.R. in US patent 6,190,701 (published: 02/20/2001) in view of Johnson, K.A. in US patent 5,376,359 (published: 12/27/1994) and Owens, J.G, in Low GWP Alternatives to HFCs and PFCs, Report of 3M Company Specialty Materials, St. Paul, MN, USA (2000) have been fully considered but are not found to be persuasive.

It is noted that the instantly applied 103 rejection does not cite Owens, therefore arguments directed to the Owens reference are rendered moot in light of the new ground of rejection.

“Applicant maintains that the hydrofluoroethers disclosed at column 2, lines 41-46 of Johnson are merely non-exemplified and speculative examples of aerosol propellants which may be used in the invention of Johnson.

Applicant points out that “[t]he specific examples of Johnson use hydrofluoroalkanes (HGAs) [HFAs] and not hydrofluoroethers [HFEs]). Therefore, there is no definite and therefore obvious teaching or suggestion in Johnson that the skilled person could or would alternatively employ a hydrofluoroether in the formulations of Roser with the expectation of arriving at the present invention with its beneficial dispersion properties” (Remarks, page 4, 2nd and 3rd paragraphs).

These arguments are not found to be persuasive. The Examiner agrees that the stabilized drug particle suspension in the Examples of Johnson use HFAs and not the claimed HFEs. However, as previously noted in the Advisory action mailed on April 28,

2010, the failure of the Examples of Johnson to disclose any of the eight hydrofluorinated ethers from the readily envisaged list of thirty liquid fluorocarbon propellants disclosed on column 2, lines 59 – 64 does not constitute a teaching away from a broader disclosure or nonpreferred embodiments or, a lack of a definite and obvious teaching or suggestion, because a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments (see MPEP 2123 [R-5]).

Furthermore, “[t]he prior art’s mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed....” In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004).

Accordingly, based on the disclosure of hydrofluoroethers by Johnson from within a readily envisaged list of about thirty fluorinated propellants, one of ordinary skill would have considered hydrofluoroethers (or hydrofluorinated ethers) as a reasonable alternative to the perfluorinated alkanes of Roser, and the hydrofluoroalkanes (HFA’s) and perfluoropolyethers disclosed in the Examples of Johnson.

Further, the Johnson reference is directed to improving the dispersion properties of suspended particles by using compositions comprising fluorinated ethers and hydrofluorinated alkanes. Accordingly, Johnson renders obvious the functional limitation in Claim 1 directed to “facilitating the dispersion property a liquid” which comprises a hydrofluorinated ether.

Applicant argues that “[t]he physical and chemical properties of these two classes of compounds (i.e., PFCs and hydrofluoroethers) differ. As an example of a simplistic comparison (non- fluorinated) which helps to demonstrate a distinction between a hydrofluoroether and a HFA, the common laboratory solvent diethyl ether ($\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$) and the identical chain-length alkane n-pentane ($\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$) have vastly different chemical and physical properties. Therefore, one skilled in the art of chemistry would not interpret prior art disclosures as indicating that n-pentane and diethyl ether confer the same or similar properties in a complex chemical system. This is because of their differing functionality, i.e., -O- against - CH_2 -, which by analogy would apply also to the fluorinated variations of these compounds.

This argument is not found to be persuasive because, although the Examiner recognizes that an ether and a corresponding alkane may have different chemical and physical properties, this argument is not relevant because the specific property claimed by Applicant, improving the dispersion properties of suspended particles, is taught by Johnson to be shared by hydrofluoroethers and hydrofluoroalkanes.

Applicant argues that “[t]he combination of one of the hydrofluoroethers disclosed in Johnson with the formulations disclosed in Roser does not provide any certainty with respect to the properties of such a combination nor an expectation of success (Remarks, page 5, 2nd paragraph).

This argument is not found to be persuasive because an obviousness rejection does not require a certainty or absolute predictability of success, only a reasonable expectation of success (see MPEP 2143.02, See, e.g., *In re O 'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)). Further, as noted in the reapplied 103(a) rejection, because the fluorocarbons of Johnson (which include hydrofluorinated ethers and polyethers) are effective at preventing aggregation/flocculation (i.e. stabilizing) suspended drug particles there would have been a reasonable expect that said ethers would also have been effective in stabilizing the drug particles in the suspension of Roser.

Applicant argues that by demonstrating the non-obviousness of the present invention over the combination of Roser and Johnson, claims 1 – 6 and 10 – 12 are allowable under the judicially created doctrine of obviousness-type double patenting over claims 1 – 4, 13, and 16 – 18 of Roser, in view of Johnson.

This argument is not found to be persuasive because, as noted above in the current 'Response to the arguments' section, claims 1 – 6 and 10 – 12 are still considered to be obvious over Roser in view of Johnson.

Finally, the Examiner points out that, contrary to Applicant's Remarks on page 5, 2nd paragraph, Claim 12 is not an independent Claim.

Conclusion

Claims 1 – 10 and 12 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DENNIS HEYER whose telephone number is (571)270-7677. The examiner can normally be reached on Monday-Thursday 8AM-5PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, BRANDON FETTEROLF can be reached at (571)272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/DENNIS HEYER/
Examiner, Art Unit 1628

/Timothy P Thomas/
Primary Examiner, Art Unit 1628